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WHITHAM, CURTIS & CHRISTOFFERSON, P.C.
11491 SUNSET HILLS ROAD
SUITE 340
RESTON, VA 20190

EXAMINER	
NGUYEN, BAO THUY L	

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/035,156
Filing Date: January 04, 2002
Appellant(s): OKADA ET AL.

Michael Whitham
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 18 August 2005 appealing from the Office action mailed 24 January 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

5,512,282	Krivan et a	04-1996
5,965,458	Kouvonen et al	10-1999
6,080,400	Williams et al	06-2000

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kouvonen et al (US Patent No. 5,965,458) in view of Williams et al (US Patent No. 6,080,400) and Krivan et al (US Patent No. 5,512,282).

Kouvonen discloses a test strip and method for rapid immunoassay of foodstuff for bacterial contaminants, for example. The test strip comprises a backing sheet and a

receiving end pad at a distance from a finishing end pad. A test membrane is provided between said pads. The membrane is intended for being brought into liquid flow contact with a sample. The test membrane preferably carries a test zone containing an immobile reagent and a control zone containing control substance. A label zone containing a mobile label is applied to the test membrane or into the absorbing pad at the receiving end, thus enabling the label to migrate to the test zone carried by liquid flow. The strip may also contain more than one test membrane in the same strip in order to test different analytes, or the same membrane may contain more than one zone each containing different reagents. The strip may also contain several different concentrations of the same reagent or label, in order to determine different analyte concentrations semiquantitatively. See abstract and column 3 through 4. Kouvonen teaches latex or metal colloid as labels, and that the test strip can be adapted for many tests including assays of foodstuff. See column 5, lines 37-47 and column 8, lines 44-67. In one specific embodiment, Kouvonen teaches a method for the detection of occult blood in a fecal sample. Kouvonen teaches a test device designed for detection both human hemoglobin and human albumin. Hemoglobin is a more specific marker of blood which can occurs after intestinal bleeding in cancer patients, for example. See column 11, example 3.

Kouvonen differs from the instant invention in failing to teach the detection of verotoxin or verotoxin producing *Escherichia coli.*

Williams discloses that verotoxin producing *Escherichia coli* causes a life-threatening blood disorder that appears within 3 - 7 days following on set of diarrhea. Symptoms of hemolytic uremic syndrome (HUS) include renal glomerular damage, hemolytic anemia, thrombocytopenia, etc. Williams discloses that ingested organisms adhere to and colonize the intestinal mucosa, where toxins are released which causes endothelial cell damage and bloody diarrhea. Williams disclose a method for the detection of bacterial toxin by a sandwich assay utilizing antibodies directed against the bacterial toxin. Williams teaches that the immobilized antibody will be present in or on a solid support and exposed to a test sample and a reporter substance in solution, which detects the presence of bound toxin. See column 4, lines 50-62; column 5, lines 20-65; and column 31, lines 4-40.

Krivan discloses that antibiotics are contraindicated in the treatment of shiga-like toxins (i.e. verotoxin) producing *Escherichia coli* infection in humans and pigs. Antibiotics actually enhance toxin production by the bacteria. Therefore, their use increases the risk of developing complications such as HUS. Column 2, lines 39-56. Krivan et al also teach the assembly of various reagents into a diagnostic kit. See column 7, lines 10-16.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the device of Kouvonen to include detection of analytes such as verotoxin or verotoxin-producing *Escherichia coli* because Kouvonen teaches that their device provides the advantages of a simple test that can be performed

anywhere and can be adapted for almost any type of analytes; and Williams and Krivan teach that the detection of verotoxin and verotoxin producing *Escherichia coli* is important because these toxins cause significant intestinal bleeding in mammals including humans. A skilled artisan would have had a reasonable expectation of success and would have been motivate to use the device of Kouvonen to detect human hemoglobin and at least verotoxin or verotoxin producing *Escherichia coli* because Krivan teaches that it is important to identify specifically which bacteria causes the symptoms observed because in some instances, standard treatment such as antibiotics, are contraindicated. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to detect hemoglobin along with either verotoxin or verotoxin producing *Escherichia coli* in the same sample because this would provide the advantage of further confirming a diagnosis of possible early onset of HUS caused by verotoxin or verotoxin producing *Escherichia coli,* thus enabling better treatment actions for the disease.

It also would have been obvious to one of ordinary skill in the art at the time the invention was made to assemble the device of Kouvonen as modified by Williams and Krivan into kits such as taught by Krivan for the advantages of convenience and economy.

Because Appellant admits that separate tests for detection of verotoxin and the bacteria that produces it are known (Specification, pages 1 and 2; and Brief, page 7, second paragraph) but are time-consuming and labor intensive, therefore, it would

have been prima facie obvious for one of ordinary skill in the art to take an obvious and well known solution to this problem, mainly, to modify a device that has been shown to be able to detect multiple analytes, such as the one taught by Kouvonen, to detect verotoxin and verotoxin producing E. Coli, or to detect hemoglobin and verotoxin, for example. Further, it would have been obvious to one having ordinary skill in the art at the time the invention was made to combine the separate tests for detection of verotoxin and the bacteria that produces it into one test, since it has been held that forming in one piece an article which has formerly been formed in two pieces and put together involves only routine skill in the art.

Even though Kouvonen teaches that it is preferable to make a test strip where all necessary reagents are incorporated therein, it would have been obvious to take a step back and separate the labeled reagent from the strip and required that it be added at whatever time that it is needed. This method is taught by both Williams and Krivan and is well known and conventional in the art.

(10) Response to Argument

Appellants brief filed 18 August 2005 have been fully considered but they are not persuasive.

In response to Appellants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Appellant argues that Kouvonen is limited to the design of a test strip and lack any discussion of detecting any particular type of analyte and that the test strip disclosed by Kouvonen is intended for generic use. Appellant argues that the substances that could be detected with the test strip of Kouvonen a laundry list of potential substances of interest and that there is no suggestion or discussion of the benefits of pairing the detection of any two particular substances. Appellant also argues that there is no showing or suggestion of the detection, on a single strip, the combination of verotoxin or verotoxin producing E. coli. Appellant further argues that the problem solved by the invention of Kouvonen is not the same as that of the instant invention.

These arguments have been fully considered but are not persuasive. It is true that Kouvonen teaches a test strip that is intended for generic and it is also true that Kouvonen does not specifically disclose the detection of verotoxin or verotoxin producing E. coli; however, contrary to Appellants arguments, Kouvonen does teach the benefits and advantages of the detection of specific analyte pairs such as hemoglobin (one of the analyte of the instant claims) and albumin or Salmonella and hormones etc. (Kouvonen, column 11, example 3) Kouvonen specifically teaches that their test strip is useful for detecting multiple analytes at the same time, either using the same test strip, or having multiple test strip banded together. Kouvonen is cited for their teaching that it is possible and well known in the art to use a test strip to simultaneously detect at least two different analytes. The discussion of assays for

verotoxin and verotoxin producing E. coli is discussed in both Williams and Krivan, and have been admitted by Appellant as well known in the art (Specification, pages 1 and 2; and Appeal Brief, page 7).

Appellant argues that the test strip of Kouvonen differ from those of the instant invention because the label taught by Kouvonen is not attached to the second immunity substances. This argument is not persuasive. Kouvonen specifically teaches blue latex particles (i.e. the label) coated with a monoclonal antibody against hCG . See Kouvonen, column 9, lines 37-41. This labeled reagent is equivalent to the instant "label attached to the second immunity substance" taught by the instant invention.

The argument that the labeled second immunity substance may be either in a mobile liquid phase or dried onto the strip is not persuasive. Throughout the Kouvonen reference, the labeled reagent is taught as being preferably coated onto the test strip. Furthermore, even though it is preferable to make a test strip where all necessary reagents are incorporated therein, it would have been obvious to take a step back and separate the labeled reagent from the strip and required that it be added at whatever time that it is needed. This method is taught by both Williams and Krivan and is well known and conventional in the art.

Appellant argues that the instant method differs from Kouvonen because it needs not be carried out on a test strip but may be carried out using a water-absorbable base material of any shape, whereas, Kouvonen specifically discloses a test strip.

This argument is not persuasive. Kouvonen teaches the limitation of a water-absorbable base material. The fact that Kouvonen called this base material a test strip does not change its water-absorbable properties. Furthermore, the instant claims do not exclude test strip, per se. Therefore, the test strip of Kouvonen is seen to be the same as the water absorbable base composition of the instant claims.

Appellant argues that Kouvonen does not teach the detection two different kinds of assay target substances. At most, Kouvonen teaches detecting two types of similar analytes such as human hemoglobin and human albumin.

This argument is not persuasive because Kouvonen clearly teaches that their test strip is useful for detecting multiple analytes at the same time regardless of whether they are different or related, Kouvonen, column 4, lines 1-9. The example taught by Kouvonen is not so limited that only related analytes can be detected using their device. The argument that Kouvonen only teaches detecting two types of similar analytes and not two different kinds of analyte as in the instant claims is not persuasive because page 7 of the instant Brief states that the instant analytes are related. Therefore, Kouvonen teaches a very similar assay to that of the instant claims.

Appellant argues that Williams does not address the same problem as that of the instant claims because the inventive feature of Williams is not the development of a new method of carrying out a diagnostic tests, but rather is an improved method of obtaining antibodies that are used in the test.

This argument is not persuasive. The fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. As stated by Appellant, tests for detecting verotoxin and the pathogen producing it are known in the art, Williams further enforces this knowledge and teaches that it is diagnostically important to accurately detect the verotoxin and teaches an improved reagent for doing so.

Appellant argues that Williams does not teach how to detect verotoxin together with another substance on the same test strip as required in the instant claims.

This argument is not persuasive. The obviousness of detecting multiple analytes on the same test strip has been clearly shown by Kouvonen. Williams is cited to demonstrate that verotoxin can be detected using an immunoassay format on the test strip of Kouvonen. Furthermore, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references.

Appellant argues that Krivan does not teach the direct detection of the bacteria producing the toxin, and only teaches that the bacterial is indirectly detected by detecting the toxin.

This argument is not persuasive. Krivan clearly teaches methods for the detection of the presence or concentration of the toxin or the presence of toxin producing bacteria in a sample using an ELISA. See Krivan, column 6, lines 52-63. Therefore, if Krivan discloses detection of SLT (i.e. verotoxin) and the bacteria

producing it, and it is well known in the art that certain strains of E. Coli produces STL (See Krivan and Williams), it logically follows that Krivan teaches detection of E. Coli . The fact that Krivan exemplifies the indirect detection of the toxin-producing bacteria does not change what is known in the art that has been specifically admitted to by Appellant. Mainly, the detection of verotoxin and verotoxin E. coli using immunoassays. It is prima facie obvious, given the knowledge that separate tests for these analytes are known, are time consuming and are complex to perform, and that immunoassay reagents are available to perform these tests, and that there exists in the art, a device that incorporates all necessary reagents for detecting multiple analytes, for an ordinary skill artisan to modify the prior art device using the prior art reagents to detect both the toxin and the bacteria producing it. Such a simplified method provides the advantage of a convenient, reliable, rapid and easy to use means for accurately detecting important pathogens and their toxins, as demonstrated by Kouvonen (column 8, lines 9-15, and lines 44-56) in view of Williams and Krivan.

Appellant argues that the combination of Kouvonen, Williams and Krivan does not provide motivation to include detection of the groups of substances recited in the instant claims since none of the three references alludes to these combinations or to any advantages that the detection of such combinations in a single test might afford.

This argument is not persuasive. Kouvonen teaches the means, motivation and advantages for detecting multiple analytes including hemoglobin; Williams teaches the means and motivation for detecting verotoxin and teaches that verotoxins are strongly

linked to E. coli O157:H7; and Krivan teaches the means and motivation for detecting verotoxin or verotoxin producing pathogen; and the instant specification admits that separate tests for these analytes are known in the art, therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the device taught by Kouvonen to detect, for example, verotoxin and verotoxin producing pathogens as taught by Williams and Krivan for the advantages of a simple, reliable, rapid and convenient test for the detection and accurately diagnoses of verotoxin and verotoxin producing pathogen.

Krivan further teaches that it is important to identify specifically which bacteria causes the symptoms observed, because in some instances standard treatment such as antibiotics are contraindicated. It also would have been obvious to one of ordinary skill in the art at the time the invention was made to detect hemoglobin along with either verotoxin or verotoxin producing *Escherichia coli* in the same sample because this would provide the advantage of further confirming a diagnosis of possible early onset of HUS (Williams, column 4) caused by verotoxin or verotoxin producing *Escherichia coli*, thus enabling better treatment actions for the disease.

Appellant argues that detection of two or more substances in the same assay or kit is a key feature of the instant invention that is not taught or contemplated by the prior art.

This argument is not persuasive because Kouvonen teaches test strips that may be adapted for many diagnostic tests where the presence or absence of some particular

compound is detected in the sample, said compound being connected to a disease or a patho-physiological state or being artificially introduced into the body (column 8, lines 9-15). Kouvonen teaches that the test strip according to their invention can be developed to detect a group of substances (polyaromatic hydrocarbons, or aflatoxins etc; column 9, lines 4-8), and further teaches that it may adapted for many tests and provides several advantages compared to traditional methods. The test is rapid, inexpensive and easy (column 8, lines 44-47). Clearly, at least one reference teaches the detection of two or more substances in the same assay or kit, and the combination of references including the admitted prior art in the specification and the Brief make obvious the instant invention for the reasons stated above.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

BAO-THUY L. NGUYEN
PRIMARY EXAMINER
3/21/06

Conferee:

LONG V. LE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

Conferee:

JAMES HOUSEL
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600